REMARKS

Applicants gratefully acknowledge the courtesy extended by the Examiner during the telephone interview of August 12, 1998.

In response to the restriction requirement set forth in the Office Action, Applicants confirm the provisional election on October 29, 1997 of the invention of group I, claims 1-4 and 7-9.

The objection to claim 7 as being in improper form is rendered moot by the cancellation of claim 7 and the presentation of new claim 31.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §112 SECOND PARAGRAPH

The Examiner rejected claims 1-4 and 7-9 under §112, second paragraph because 1) the method of claim 8 does not recite a step in which the protein is collected or obtained and 2) the phrase "consisting essentially of" is vague and indefinite as it is not known what parameters of the polynucleotide can be changed.

In reply, Applicants submit that these rejections are rendered moot by the amendments to the claims presented herein.

REJECTIONS OF THE CLAIMS UNDER 35 U.S.C. §102(e)

The Examiner rejected claims 1, 2 and 7-9 under §102(e) as being anticipated by the disclosure in Reyes et al. U.S. Patent No. 5,686,239 of DNA molecules encoding ORF2, of HEV vectors comprising those sequences, of host cells comprising those vectors, and of methods of making those proteins. Applicants respectfully traverse this rejection.

The newly added claims are directed to DNA molecules having a sequence consisting of the nucleotides which encode amino acid 112 to amino acids 578-607 of an HEV ORF2 protein.

By comparison Reyes et al. disclose nucleic acid sequence which encodes the full length 660 ORF2 protein of HEV of the Burma and Mexican strains of HEV (see SEQ. ID. Nos. 15 and 16) and ORF2 fragments which encode 42 (SEQ ID. Nos. 11 and 12) and 327 (SEQ ID. Nos. 13 and 14) carboxy terminal amino acids (amino acids 334 to 660) of ORF2. Thus, as Reyes does not disclose the DNA molecules presently claimed, Reyes cannot be held to anticipate claims 25-32.

Accordingly, withdrawal of this rejection is respectfully requested.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §102(b)

Claims 1-4 are rejected under §102(b) as being anticipated by Tsarev (1992 PNAS 89:559-563). With all due respect, Applicants disagree.

Tsarev et al. refer to the sequencing of virtually the entire genome of the SAR55 strain of hepatitis E and disclose that the sequences reported have been deposited in the GenBank database under accession numbers M80581 and M81415. Nowhere does Tsarev disclose or teach the specific DNA molecules now claimed, namely DNA sequences which encode from amino acid 112 to amino acids 578-607 of an HEV ORF2 protein. Withdrawal of the §102(b) rejection is therefore respectfully requested.

Claims 1-4 and 7-9 are also rejected under §102(b) as being anticipated by Tsarev et al. (J. Infectious Dis. 168:369-378) and by WO94/06913 of Tsarev.

Applicants respectfully traverse this rejection.

Figure 1 of the Tsarev publication discloses an expression vector designated p63-2 which contains the entire open reading frame 2 of the SAR55 HEV genome. WO94/06913 also discloses the construction of the vector p63-2 (Figure 1)and the infection of insect cells with this vector. As the entire ORF2 sequence encodes a protein 660 amino acids in length, the expression vector shown in Figure 1 of the Tsarev et al. publication and in WO 94/06913, and its use in a method of expression, cannot be held to anticipate DNA molecules which encode from amino acid 112 to amino acids 578 to 607 of an HEV ORF2 protein.

Claims 1-3 and 7-9 are rejected under §102(b) as being anticipated by He et al. (1993 J. Clin. Microbiol. 31:2167-2173). He et al. is cited by the Examiner as disclosing DNA molecules comprising sequence encoding amino acids 112 to 607 of the HEV ORF2 protein.

In reply, Applicants note that the ORF2 expression vector contained in He et al. contains sequence encoding the complete 660 amino acid ORF2 protein and therefore cannot be held to anticipate DNA molecules which encode from amino acid 112 to amino acids 578 to 607 of an HEV ORF2 protein as claimed in the present application. Withdrawal of this rejection is therefore respectfully requested.

Claims 1, 2 and 7-9 are also rejected under §102(b) as being anticipated by Li et al. (1994) J. Clin. Microbiol., 32:2060-2066), He et al. (1995) J. Clin. Microbiol., 33:3308-3311), Panda et al. (1995) J. Clin. Microbiol., 33:2653-2659), and WO 95/08632. The Examiner asserts that all of the cited references disclose DNA molecules comprising a sequence encoding

HEV ORF2 protein, vectors comprising those sequences, host cells comprising those vectors, and methods of expressing the proteins. Applicants respectfully traverse this rejection.

Li et al. disclose the expression of fusion proteins which contain portions of HEV ORF2 and ORF3. The two ORF2-containing fusion proteins are designated ORF2.1 and ORF2.2 and, as disclosed in the last paragraph of page 2063 of Li, the ORF2.1 protein contains the carboxy terminal 1/3 of the coding sequence from ORF2 (i.e., amino acids 440 to 660) and the ORF2.2 protein contains an N-terminal extension of 294 amino acids over the 2.1 protein. (i.e., amino acids 146-660 of ORF2)

By comparison, the claims are directed to DNA molecules which encode from amino acid 112 to amino acids 578 to 607 of HEV ORF2. Thus the claimed DNA molecules are completely distinct from the sequences disclosed in Li et al..

With respect to He et al., this reference discloses the construction of an expression vector containing the entire ORF2 sequence (see paragraph bridging left and right columns of page 3308) and the use of this expression vector to produce a full length structural protein in insect cells. Thus, since the sequence of He et al. encodes amino acids 1 to 660 of ORF2, it does not anticipate the claimed DNA molecules.

Turning to Panda et al., this reference discloses the expression in E. coli of the full-length ORF2 as a fusion with an N-terminal hexahistidine sequence (see first paragraph of page 2654 which discloses that, for protein expression, a DNA fragment encompassing the complete ORF2 was cloned in a prokaryotic expression vector). Thus, the claims cannot be held to be anticipated by Panda et al.

Finally, WO95/08632 describes the construction of expression vectors (Figures 5 and 6, Example 2) which encode the full length 660 amino acid ORF2 protein (pGEX1-AC2), ORF2 amino acids 338-660 (pGEX1-AC2.1), ORF2 amino acids 98-660 (pGEX1-AC2.2), ORF2 amino acids 1-150 (pGEX1-AC2.3) and ORF2 amino acids 1-260 (pGEX1-AC2.4) (see page 27, lines 3-13). Thus, none of the expression vectors disclosed in WO95/08632 encode from amino acid 112 to amino acids 578-607 of an HEV ORF2 protein as disclosed and claimed in the present application.

In sum, in view of the above remarks, withdrawal of the §102(b) rejections is respectfully requested.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §102(a)

Claims 1, 2 and 7-9 are rejected under §102(a) as being anticipated by the disclosure in WO 96/12807 of DNA molecules comprising sequences encoding the C- terminal portion of an HEV ORF2 protein, vectors comprising those sequences, host cells comprising those vectors, and methods of expressing those proteins.

As noted above, the present claims are directed to DNA sequences which encode from amino acid 112 to amino acids 578-607 of the full-length 660 amino acid ORF2 protein.

By comparison, WO96/12807 discloses expression vectors which encode 3 ORF2 proteins: 1) the 42 carboxy-terminal amino acids of ORF2 (amino acids 619-660), 2) the 327 carboxy-terminal amino acids of ORF2 (amino acids 334-660) and 3) the 549 carboxy-terminal amino acids of ORF2 (amino acids 112-660). Thus, it is readily apparent that none of the DNA sequences contained in the ORF2 expression vectors of WO96/12807 encodes from amino acid

112 to amino acids 578-607 of an HEV ORF2 protein. Accordingly, withdrawal of the §102(a) rejection of the claims is respectfully requested.

In view of the above amendments and remarks, Applicants respectfully submit that the instant application is in condition for allowance.

Early and favorable consideration by the Examiner is respectfully solicited.

Respectfully submitted,

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